WHAT IS CLAIMED IS:

1. A method for identifying an agent that alters processing of β-amyloid precursor protein (APP) comprising:

contacting the agent with an animal host cell that expresses APP and at least one APP processing enzyme, and

detecting altered APP processing to identify the agent that alters the processing of APP.

2. The method of claim 1, wherein detecting the altered APP processing comprises assessing the relative presence or absence of at least one species of APP fragment on the surface of the host cell.

3. The method of claim 2, wherein the at least one species of APP fragment is APPs-α, APPs-β, or APPs-γ.

4. The method of claim 1, wherein the at least one APP processing enzyme is α-secretase, β-secretase, or γ-secretase.

5. The method of claim 1, wherein the altered APP processing results in a decreased production of an amyloid β-protein (Aβ).

6. The method of claim 5, wherein the amyloid β-protein is associated with an increased risk of Alzheimer's disease.

7. The method of claim 6, wherein the amyloid β protein associated with an increased risk of Alzheimer's disease is Aβ1-39, Aβ1-40, or Aβ1-42.

8. The method of claim 1, wherein the agent is from a compound library.

9. The method of claim 8, wherein the compound library is a combinatorial chemical library.

10. The method of claim 8, wherein the compound library is a natural products library.

11. The method of claim 8, wherein the compound library is a peptide library.

12. The method of claim 1, wherein the agent is a small molecule.

13. The method of claim 1, wherein the agent is a biomolecule.

14. The method of claim 13, wherein the biomolecule is a peptide.

15. The method of claim 14, wherein the peptide is produced by transcription and translation from an oligonucleotide encoding the peptide.

16. The method of claim 15, wherein the oligonucleotide has a length of about 18 to about 120 nucleotides.

17. The method of claim 15, wherein the oligonucleotide has a length of about 36 to about 60 nucleotides.

18. The method of claim 15, wherein the contacting of the peptide with the host cell comprises introducing an expression vector, the expression vector comprising the oligonucleotide encoding the peptide, into the host cell, the host cell thereby expressing and displaying the peptide within a secretory pathway and on an extracellular cell surface.

19. The method of claim 15, wherein the oligonucleotide is from an expression library comprising a plurality of oligonucleotides, at least of majority of the oligonucleotides having different sequences encoding different peptides.

20. The method of claim 19, wherein the sequence of the plurality of oligonucleotides is randomized.

21. The method of claim 19, wherein the expression library is pre-enriched for oligonucleotides encoding peptides that specifically bind to APP.

22. The method of claim 19, wherein the contacting of the peptide with the host cell comprises introducing the expression library into a first plurality of animal host cells that express APP and at least one APP processing enzyme, the host cells thereby expressing and displaying the different peptides within a secretory pathway and on an extracellular cell surface.

23. The method of claim 22, further comprising:

selecting from the first plurality of host cells displaying the different peptides a first subset of host cells that exhibit altered APP processing; and

identifying from the first subset of host cells a first sub-library of the expression library comprising at least one oligonucleotide that encodes the peptide that alters the processing of APP.

24. The method of claim 22, wherein the first plurality of host cells displaying the different peptides have been enriched using a selectable marker.

25. The method of claim 24, wherein the selectable marker is V5, FLAG, or thioredoxin.

26. The method of claim 24, wherein the enrichment comprises magnetic bead selection.

27. The method of claim 24, wherein the enrichment comprises selection by fluorescence-activated cell sorting.

28. The method of claim 24, wherein the host cells expressing and displaying the different peptides on the extracellular cell surface express a high copy number of the different peptides.

29. The method of claim 15, wherein the peptide is displayed as a

fusion protein with a presentation molecule.

30. The method of claim 29, wherein the presentation molecule is CD24.

31. The method of claim 29, wherein the presentation molecule is IL-3 receptor.

32. The method of claim 29, wherein the presentation molecule is thioredoxin.

33. The method of claim 29, wherein the fusion protein further comprises a marker epitope.

34. The method of claim 33, wherein the marker epitope is polyhistidine, V5, FLAG, or myc

35. The method of claim 29, wherein the fusion protein further includes a signal for a glycophosphatidylinositol (GPI) anchorage.

36. The method of claim 1, wherein the animal host cell is a mammalian host cell.

37. The method of claim 1, wherein the animal host cell is a recombinant host cell.

38. The method of claim 37, wherein the animal host cell is an isolated cell.

39. The method of claim 1, wherein the agent is contacted with the host cell under substantially physiological conditions.

40. The method of claim 39, wherein the substantially physiological conditions comprise the presence of a complex biological fluid.

41. The method of claim 40, wherein the complex biological fluid is blood, serum, plasma, or cerebral spinal fluid (CSF).

42. The method of claim 2, wherein the assessment of the relative presence or absence of at least one species of APP fragment on the cell surface comprises contacting the host cell with at least one detectably labeled marker that specifically binds to the at least one species of APP fragment and detecting the bound, labeled marker.

43. The method of claim 42, wherein the at least one marker is an antibody that binds to a predetermined epitope of APP or APP fragment.

44. The method of claim 43, wherein the assessment of the relative presence or absence of at least one species of APP fragment on the cell surface further comprises determining a ratio of the detection signals of at least two labeled antibodies specific for at least two different epitopes of APP or an APP fragment.

45. The method of claim 1, wherein the agent is an allosteric effector of APP.

46. The method of claim 1, wherein the detecting altered APP processing on the surface of the host cell comprises the use of a flow sorter.

47. The method of claim 1, further comprising administering the agent to an animal and monitoring the animal for an effect on a physiological condition associated with altered APP processing.

48. The method of claim 47, wherein the administration is by direct injection or by oral administration.

49. The method of claim 47, wherein the agent is a peptide and the animal is a transgenic mouse comprising an expression construct that encodes the peptide, wherein the expression construct comprises, in operative combination, (a) a promoter, (b) a secretory sequence, (c) a nucleotide sequence encoding the peptide, and (d) a transcription termination sequence; and wherein the transgenic mouse expresses detectable levels of the peptide *in vivo*.

50. The method of claim 49, wherein the expression construct encodes a

presentation molecule that is anchored to a cell membrane, the expression construct further comprising

(e) a nucleotide sequence encoding a presentation protein, said presentation protein-encoding sequence located 3' to the peptide-encoding sequence, and

(f) a nucleotide sequence encoding a transmembrane domain or a GPI linker, said transmembrane domain or GPI linker sequence located 3' to the presentation protein-encoding sequence and 5' to the transcription termination sequence.

51. The method of claim 47, wherein the effect on a physiological condition associated with altered APP processing is a decrease in the levels of Aβ protofibrils or Aβ40/42.

52. The method of claim 47, wherein the effect on a physiological condition associated with altered APP processing is plaque inhibition.

53. A method for identifying a peptide that alters processing of β-amyloid precursor protein (APP) comprising:

introducing an expression library comprising a plurality of oligonucleotides, at least a majority of the oligonucleotides having different sequences encoding different peptides, into a first plurality of animal host cells that express APP and at least one APP processing enzyme, the host cells thereby expressing and displaying the different peptides within a secretory pathway and on an extracellular cell surface;

selecting from the first plurality of host cells displaying the different peptides a first subset of host cells that exhibit altered APP processing; and

identifying from the first subset of host cells a first sub-library of the expression library comprising at least one oligonucleotide that encodes the peptide that alters the processing of APP.

54. The method of claim 53, wherein the animal host cell is a mammalian host cell.

55. The method of claim 53, wherein the animal host cell is a recombinant host cell.

56. The method of claim 53, wherein the animal host cell is an isolated cell.

57. The method of claim 53, wherein the first plurality of host cells display the different peptides under substantially physiological conditions.

58. A method for identifying a peptide that alters processing of β-amyloid precursor protein (APP) comprising:

(1) pre-enriching an expression library comprising a plurality of oligonucleotides, at least a majority of the oligonucleotides having different sequences encoding different peptides, for at least one oligonucleotide that encodes a peptide that specifically binds to APP, the pre-enrichment comprising the steps of

(a) introducing the expression library into a phage display vector which can express the peptides encoded by the oligonucleotide sequences on the surface of the phage;

(b) expressing the different peptides on the surface of the phage;

(c) selecting a subset of phage particles that express peptides that specifically bind APP or an N-terminally truncated APP, said N-terminally truncated APP having the α- or β-secretase cleavage site; and

(d) recovering the oligonucleotide sequences from the selected phage particles to form a pre-enriched expression library;

(2) introducing the pre-enriched expression library into a first plurality of animal host cells that express APP and at least one APP processing enzyme, the host cells thereby expressing and displaying the at least one APP-binding peptide within a secretory pathway and on an extracellular cell surface;

(3) selecting from the first plurality of host cells displaying the at least one APP-binding peptide a first subset of host cells that exhibit altered APP processing; and

(4) identifying from the first subset of host cells a first sub-library of the pre-enriched expression library comprising at least one oligonucleotide that encodes the peptide that alters the processing of APP.

59. A method for identifying a peptide that alters processing of β-amyloid precursor protein (APP) comprising:

introducing an expression library comprising a plurality of oligonucleotides, at least a majority of the oligonucleotides having different sequences encoding different peptides, into a first plurality of animal host cells that express APP and at least one APP processing enzyme, the host cells thereby expressing and displaying the different peptides within a secretory pathway and on an extracellular cell surface;

selecting from the first plurality of host cells displaying the different peptides a first subset of host cells that exhibit altered APP processing; wherein the altered APP processing is determined by assessing the relative presence or absence of at least one species of APP fragment on the surface of the host cells displaying the different peptides by contacting the host cells with at least one detectably labeled marker that specifically binds to the at least one species of APP fragment and detecting the bound labeled marker; and

identifying from the first subset of host cells a first sub-library of the expression library comprising at least one oligonucleotide that encodes the peptide that alters the processing of APP.

60. A method for identifying a peptide that alters processing of β-amyloid precursor protein (APP) comprising:

introducing an expression library comprising a plurality of oligonucleotides, at least a majority of the oligonucleotides having different sequences encoding different peptides, into a first plurality of animal host cells that express APP and at least one APP processing enzyme, the host cells thereby expressing and displaying the different peptides within a secretory pathway and on an extracellular cell surface under substantially physiological conditions;

selecting from the first plurality of host cells displaying the different peptides a first subset of host cells that exhibit altered APP processing; wherein the altered APP processing is determined by assessing the relative presence or absence of at least one species of APP fragment on the surface of the host cells displaying the different peptides

by contacting the host cells with at least one detectably labeled marker that specifically binds to the at least one species of APP fragment and detecting the bound labeled marker; and

identifying from the first subset of host cells a first sub-library of the expression library comprising at least one oligonucleotide that encodes the peptide that alters the processing of APP.

61. The agent identified by the method according to claim 14, wherein the agent is converted into a peptidometic, a isosteric replacement compound, a D-amino acid analog, or a non-peptidyl compound.

62. The agent identified by the method according to claim 1, wherein the agent is modified to facilitate passage through the blood brain barrier.

63. The agent identified by the method according to claim 1, wherein the agent is formulated for parenteral, oral, sustained release, topical, intranasal or inhalation use.